

## Complete Summary

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### GUIDELINE TITLE

Evidence-based care guideline for necrotizing enterocolitis (NEC) among very low birth weight infants.

### BIBLIOGRAPHIC SOURCE(S)

Cincinnati Children's Hospital Medical Center. Evidence-based care guideline for necrotizing enterocolitis (NEC) among very low birth weight infants. Cincinnati (OH): Cincinnati Children's Hospital Medical Center; 2005 Jul 14. 12 p. [91 references]

### GUIDELINE STATUS

This is the current release of the guideline.

## COMPLETE SUMMARY CONTENT

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 METHODOLOGY - including Rating Scheme and Cost Analysis  
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## SCOPE

### DISEASE/CONDITION(S)

Necrotizing enterocolitis (NEC)

### GUIDELINE CATEGORY

Diagnosis  
 Evaluation  
 Management  
 Prevention  
 Treatment

## CLINICAL SPECIALTY

Family Practice  
Gastroenterology  
Nutrition  
Pediatrics  
Surgery

## INTENDED USERS

Advanced Practice Nurses  
Allied Health Personnel  
Health Care Providers  
Nurses  
Patients  
Physician Assistants  
Physicians

## GUIDELINE OBJECTIVE(S)

- To provide evidence based recommendations for the evaluation and management of necrotizing enterocolitis (NEC) among very low birth weight infants
- To improve diagnostic accuracy, treatment outcomes, and patient/parent satisfaction

## TARGET POPULATION

Preterm infants less than 1500 grams birth weight

This guideline is not intended for use in:

- Term and near term infants
- Infants with major congenital anomalies (e.g., congenital heart disease, Trisomy 21)

## INTERVENTIONS AND PRACTICES CONSIDERED

### Prevention

1. Encourage mothers to supply breast milk
2. Consider donor milk, if mother's milk is unavailable

Note: Guideline developers considered but did not find sufficient evidence to make recommendations on the following preventive interventions:

- Minimal enteral feeding
- Early or delayed initiation of feeding
- Specific rate of feeding volume
- Transpyloric versus gastric feeding
- Bolus versus continuous feeding

- Specific location for umbilical artery catheters
- Probiotics
- Acidification of feeds
- Supplemental vitamin E
- Prenatal and postnatal indomethacin

Note: No preventive benefits have been shown for amino acid supplementation, immunoglobulins, and antibiotics

## Diagnosis/Evaluation

1. Bell's necrotizing enterocolitis (NEC) staging system
2. Abdominal radiograph

Note: Guideline developers considered but did not find sufficient evidence to make recommendations for the following measures: using stool patterns, presence of occult blood or presence of specific pathogens as indicators of NEC risk, or gastric residuals as a predictor of necrotizing enterocolitis.

## Treatment

1. Medications - antibiotics

Note: There is insufficient evidence on benefit or risk regarding choice of antibiotic regimen or duration of treatment

2. Nutrition

Note: There is insufficient evidence on benefit or risk regarding the timing of reinitiating feeding

3. Abdominal paracentesis

## Surgical Management

1. Transfer neonates with suspected necrotizing enterocolitis to a facility that can meet their surgical needs
2. Evaluation by surgeon
3. Base surgical intervention decisions on both the clinical and radiologic presentation
4. Percutaneous drainage versus exploratory laparotomy

## MAJOR OUTCOMES CONSIDERED

- Diagnostic accuracy
- Efficacy of interventions at decreasing the risk of or preventing necrotizing enterocolitis
- Risks and rates of necrotizing enterocolitis
- Benefits and risks of treatment interventions
- Patient/parent satisfaction

## METHODOLOGY

### METHODS USED TO COLLECT/SELECT EVIDENCE

#### Searches of Electronic Databases

### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Cincinnati clinicians responsible for the care of patients with necrotizing enterocolitis (NEC) were asked to submit clinical questions using the PICO (patient, intervention, comparison, outcome) format. Using these questions as guides, two independent computerized, OVID, literature searches of Medline and the Cochrane databases were performed (BH and ED). Searches employed a combination of Boolean searching on human-indexed thesaurus terms (Medical Subject Heading [MeSH] headings using an OVID Medline interface) and "natural language" searching on words in the title, abstract, and indexing terms. The citations were reduced by eliminating duplicates, most review articles, non-English articles, and articles on NEC in adults. The resulting abstracts were reviewed by a methodologist to eliminate low quality citations.

The following search strategies were used: Necrotizing enterocolitis as a phrase in the title or as a subject heading was combined with established filters for clinical articles in the diagnosis, therapy, etiology, or prognosis domains. The search was limited to human, English, infants as an age group, and 1980 to May 2003. During the course of the guideline development, additional clinical questions were generated and subjected to the search process.

Titles and abstracts of the identified citations (619) were initially categorized independently by two guideline team leaders as definitely included in guideline development (all randomized controlled trials [RCTs], all meta-analyses, all systematic reviews and all observational studies with comparison groups, and sample sizes greater than 50), definitely not included (case reports, letters, observational studies without control groups, and/or sample size less than 30) and those possibly included. Studies in the included and possibly included categories were re-reviewed by the methodologist and other guideline team members to assure that studies to be appraised in detail were relevant to the clinical questions that were used to develop search terms. Complete copies of the remaining articles were organized by question and distributed to the team according to each member's expressed interest and area of expertise. All selected studies were appraised by the methodologist and at least two team members using a standardized form for evaluating design, sample size, methods, and findings.

### NUMBER OF SOURCE DOCUMENTS

619

### METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Not stated

## RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

## METHODS USED TO ANALYZE THE EVIDENCE

Review  
Review of Published Meta-Analyses

## DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

## METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

## DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

During formulation of these guidelines, the team members have remained cognizant of controversies and disagreements over the management of these patients. They have tried to resolve controversial issues by consensus where possible and, when not possible, to offer optional approaches to care in the form of information that includes best supporting evidence of efficacy for alternative choices.

## RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

## COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

## METHOD OF GUIDELINE VALIDATION

External Peer Review  
Internal Peer Review

## DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guideline development process has been reviewed and approved by clinical experts not involved in the development process, senior management, Risk Management & Corporate Compliance, the Institutional Review Board, other appropriate hospital committees, and other individuals as appropriate to their intended purposes.

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

Each recommendation is followed by evidence classification (A-X) identifying the type of supporting evidence. Definitions for the types of evidence are presented at the end of the "Major Recommendations" field.

#### Prevention

##### Type of Milk

1. It is recommended that mothers of infants at risk for necrotizing enterocolitis (NEC) be encouraged to supply breast milk as the optimal enteral nutrition to decrease risk. Infants who received human milk were 4 times less likely to have confirmed NEC compared to infants who received formula (relative risk [RR] 0.25, 95% confidence interval [CI\*] 0.06 to 0.98) (McGuire & Anthony, "Formula milk versus term human milk," 2003 [M]; Schanler et al., 1999 [A]; Lucas & Cole, 1990 [A]; Gross, 1983 [B]; Tyson et al., 1983 [B]; Svenningsen, Lindroth, & Lindquist, 1982 [B]).

Note 1: Studies show that providing human milk to twenty preterm infants will prevent one case of NEC (McGuire & Anthony, "Formula milk versus preterm human milk," 2003 [M]).

Note 2: Although the benefits of human milk to decrease NEC risk have been demonstrated primarily with donor milk, it is reasonable to encourage use of mother's own milk (Local Expert Consensus [E]).

Note 3: Conditions that would contraindicate the use of breast milk are detailed in the Pediatric Nutrition Handbook 5th Ed. American Academy of Pediatrics (Kleinman, 2004 [O]).

\*95%CI: 95% Confidence Interval expresses the uncertainty (precision) of a measured value; it is the range of values within which we can be 95% sure that the true value lies. A study with a larger sample size will generate more precise measurements, resulting in a narrower confidence interval.

2. It is recommended that donor milk be considered, if available and affordable, as an alternative, when mother's own milk is unavailable (Local Expert Consensus [E]).

Note 1: Current cost of donor milk is 4 to 5 times higher than formula designed for premature infants.

Note 2: When recommending the use of donor milk, reimbursement issues may need to be considered and discussed with the family. Donor milk may not be covered by insurance. For more information see [www.hmbana.com](http://www.hmbana.com).

##### Feeding Strategies

Available studies were reviewed for use of minimal enteral feeds, timing of initiation of feeds, and rates for advancing feeds (see Table below).

Table: Definitions Used in Studies of Feeding Issues

Minimal Enteral Feeding	<p>Dilute or full strength formula feedings providing &lt;25 kcal/kg/day (37cc/kg/day) for &gt;5 day (Tyson &amp; Kennedy, 2003 [M])</p> <p>0.5 to 1 mL/hr to extubation (McClure &amp; Newell, 2000 [A])</p> <p>20 mL/kg/day, day 4 to 14 (Schanler et al., 1999 [A]) In all studies, controls were not fed by mouth</p>
Timing of Initiation of Feeds	<p>Definitions of early versus late initiation varied among studies reviewed.</p> <p>Early -- day 1 to 5</p> <p>Late -- day 5 to 14 (Kennedy, Tyson, &amp; Chamnanvanikij, "Early versus delayed," 2003 [M])</p>
Rate of Advancement of Feeds	<p>Rates of advancement varied with overlapping categories from study to study</p> <p>10-20 cc/kg/day slow</p> <p>20-35 cc/kg/day fast (Kennedy, Tyson, &amp; Chamnanvanikij, "Rapid versus slow," 2003 [M])</p> <p>20 mL/kg/day X 10 day versus increase by 20 mL/kg/day to 140 mL/kg/day (Berseth, Bisquera, &amp; Paje, 2003 [A])</p>

#### Minimal Enteral Feeding

3. There is insufficient evidence regarding the role of minimal enteral feedings in preventing NEC.

Note 1: A meta-analysis reviewing 6 studies showed use of minimal feeds had no effect on risk of NEC (Tyson & Kennedy, 2003 [M]).

Note 2: Inclusion of two additional randomized controlled trials (RCTs) did not alter results of the meta-analysis (McClure & Newell, 2000 [A]; Schanler et al., 1999 [A]).

#### Timing of Initiation of Feeds

4. There is insufficient evidence to support either early or delayed initiation of feeding relative to risk for NEC (Kennedy, Tyson, & Chamnanvanikij, "Early versus delayed," 2003 [M]; Wilson et al., 1997 [A]; LaGamma, Ostertag, & Birenbaum, 1985 [C]; McKeown et al., 1992 [D]).

#### Rate of Advancement of Feeds

5. There is insufficient evidence to recommend a specific rate of feeding volume advancement in relation to NEC risk.

Note 1: No difference in NEC risk was observed in studies advancement as low as 10 cc/kg/day and as high as 35 cc/kg/day (Kennedy, Tyson, & Chamnanvanikij, "Rapid versus slow," 2003 [M]; Kamitsuka, Horton, & Williams, 2000 [D]).

Note 2: One large study showed a decreased rate of NEC in infants maintained at 20 cc compared to those children advanced. Inclusion of this study did not alter results of the meta-analysis (Berseth, Bisquera, & Paje, 2003 [A]).

#### Transpyloric Versus Gastric Feeding

6. There is insufficient evidence to support either transpyloric or gastric feeding methods relative to the risk of NEC (McGuire & Anthony, "Formula milk versus term human milk," 2003 [M]).

#### Bolus Versus Continuous Feeding

7. There is insufficient evidence to support either bolus or continuous tube feeding as a method to reduce the risk of NEC (Premji & Chessell, 2003 [M]).

#### Umbilical Artery Catheters (UAC)

8. There is insufficient evidence to recommend a specific placement location for the tip of the umbilical artery catheter. Umbilical artery catheter position (high versus low) has not been found to effect the incidence of NEC (Barrington, 2003 [M]).
9. There is insufficient evidence to evaluate the risk of NEC associated with enteral feeding while an umbilical artery catheter is in place.

Note: One small randomized trial found no difference in the incidence of NEC between infants fed early, with a UAC in place, and those in which feeds were delayed until 24 hours after UAC removal (Davey et al., 1994 [B]).

#### Probiotics

10. There is insufficient evidence to recommend either use or avoidance of probiotics. Clinical trials of the effects of probiotics on the risk of NEC have not consistently shown benefit.

Note 1: One large observational study showed a significant decrease in NEC compared to historical controls when infants were treated with lactobacillus and bifidobacterium (Hoyos, 1999 [D]).

Note 2: One large RCT of lactobacillus GG found no significant effect on the incidence of NEC in very low birth weight (VLBW) infants (Dani et al., 2002 [A]).



Note 3: A second large RCT of lactobacillus and bifidobacterium in VLBW infants found a significant reduction in NEC incidence among treated infants (Lin et al., 2005 [A]).

Note 4: Issues regarding the safety of probiotic use in immunodeficient hosts such as preterm infants have been raised, particularly the potential for sepsis. None of the clinical trials reported harmful side effects although they were not powered to evaluate safety (Land et al., 2005 [O]).

## Additional Prevention Strategies

11. The following prevention strategies have been evaluated in large sample size, randomized, controlled trials or meta-analyses with no statistically significant effects on NEC risk.

### Amino Acid Supplementation

- Enteral glutamine (Vaughn et al., 2003 [A])
- Intravenous (IV) glutamine (Poindexter et al., 2004 [A])
- Enteral arginine (Amin et al., 2002 [A])

### Immunoglobulins

- Oral immunoglobulin G (IgG) or IgA/IgG combination (Foster & Cole, 2003 [M]; Rubaltelli, Benini, & Sala, 1991 [A]; Eibl et al., 1988 [A])  
Note: There is no RCT of IgA alone for the prevention of NEC.
- Intravenous IgG (Fanaroff et al., 1994 [A])

### Antibiotics

- Results from a meta-analysis of 5 studies suggest that oral aminoglycosides decrease the incidence of NEC. However, lack of information on other outcomes including mortality and development of resistant bacteria precludes any recommendation (Bury & Tudehope, 2003 [M]).
- Oral or intravenous erythromycin (Ng & Shah, 2003 [M])

Where evidence is present but sparse, information is shared below for purposes of awareness even if conclusions can not be made.

### Acidification of Feeds

12. One small RCT showed that acidification of feeds was associated with decreased risk of NEC (Carrion & Egan, 1990 [B]). Based on the small sample size, no recommendation can be made.

### Supplemental Vitamin E

13. In those at greatest risk for NEC, studies suggest that supplemental vitamin E may increase the risk of NEC with no effect on other outcomes with the exception of risk of severe retinopathy of prematurity, which may be less

(Brion, Bell, & Raghuveer, 2003 [M]; Johnson et al., 1985 [A]; Finer et al., 1984 [D]).

#### Prenatal Indomethacin

14. There is insufficient evidence to recommend either use or avoidance of prenatal indomethacin related to risk of NEC (Parilla et al., 2000 [D]; Vermillion & Newman, 1999 [D]; Major et al., 1994 [D]; Norton et al., 1993 [D]).

#### Postnatal Indomethacin

15. Evidence does not support an altered risk of NEC with use of indomethacin for prevention of intraventricular hemorrhage (Fowlie & Davis, 2003 [M]) or treatment of patent ductus arteriosus (PDA) (Malviya, Ohlsson, & Shah, 2003 [M]; Gersony et al., 1983 [A]; Cooke & Embleton, 2000 [S]).

Note 1: Although the number of infants <1,000 g birth weight was small, a collaborative trial showed no difference on NEC risk using surgical versus indomethacin treatment for patent ductus arteriosus (PDA). (Gersony et al., 1983 [A]).

Note 2: No difference in NEC risk has been noted between ibuprofen and indomethacin used for patent ductus arteriosus treatment or prevention (Shah & Ohlsson, 2003 [M]).

### Medical Management

#### Evaluation

#### Clinical Assessment and Diagnosis

1. Bell's NEC staging system is commonly used to assess NEC severity (Bell et al., 1978 [C]). Studies to firmly establish assessment and diagnosis criteria are not available (see Table below).

Table: Bell's Staging for NEC

Stage I: Suspect	Stage II: Definite	Stage III: Advanced
Any one or more historical factors producing perinatal stress	Any one or more historical factors	Any one or more historical factors
Systemic manifestations--temperature instability, lethargy, apnea, bradycardia	Signs and symptoms as in Stage I plus persistent occult or gross gastrointestinal bleeding; marked abdominal distention	Signs and symptoms and in Stage II plus deterioration of vital signs, evidence of septic shock, or marked gastrointestinal hemorrhage
Gastrointestinal manifestations--poor	Abdominal radiographs show significant intestinal	Abdominal radiographs may show

Stage I: Suspect	Stage II: Definite	Stage III: Advanced
feeding, increasing pre-gavage residuals, emesis (may be bilious or test positive for occult blood), mild abdominal distention, occult blood may be present in stool (no fissure)	distension with ileus; small bowel separation (edema in bowel wall or peritoneal fluid), unchanging or persistent "rigid" bowel loops, pneumatosis intestinalis, portal vein gas	pneumoperitoneum in addition to signs listed for Stage II
Exclude other disorders via bacterial cultures, electrolyte analysis, maternal drug history, coagulation studies, and contrast studies		

## Diagnostics

### Laboratory Studies

2. While specific pathogens have been isolated from stools and abdominal fluid during outbreaks of NEC, no specific pathogen has been found to have a consistent causal relationship with NEC (de la Cochetiere et al., 2004 [C]; Peter et al., 1999 [C]; Millar et al., 1996 [C]; Rotbart et al., 1988 [C]; Blakey et al., 1985 [C]; Thomas et al., 1984 [C]; Gupta, Burke, & Herson, 1994 [D]; Keller et al., 1991 [D]; Sherertz & Sarubbi, 1982 [D]).
3. There is insufficient evidence to support the use of stool patterns, presence of occult blood, or presence of specific pathogens as clinical indicators of NEC risk (Peter et al., 1999 [C]; Abramo et al., 1988 [C]; Andrews & Krowchuk, 1997 [D]).
4. There is insufficient evidence for use of gastric residuals as a predictor of NEC. Gastric residuals in infants who developed NEC tended to be larger, but significant overlap in the amount of residual precludes its use as a marker for NEC (Cobb, Carlo, & Ambalavanan, 2004 [D]).

### Radiologic Studies

5. It is recommended that an abdominal radiograph be performed in infants with clinical suspicion of NEC (Bell et al., 1978 [C]). The influences on infant outcome and diagnostic validity of the number of abdominal x-rays, the type of view(s), or the frequency or timing of abdominal radiographs have not been systematically studied.

Note 1: Inter-observer reliability of radiographic signs of NEC is low (Napoli et al., 2004 [D]).

Note 2: While positive radiographic findings have good predictive value, negative studies must be interpreted with caution (Tam, Camberos, & Applebaum, 2002 [D]; Kosloske, 1994 [D]).

## Intervention

## Medications

1. There is insufficient evidence on benefit or risk regarding choice of antibiotic regimens or duration of antibiotic treatment of NEC (Faix, Polley, & Grasela, 1988 [B]; Scheifele et al., 1987 [C]).

Note: Decisions regarding antibiotic choice and duration might best be guided by:

- Culture results
- Antibiotic resistance patterns present within nurseries

(Local Expert Consensus [E])

2. There is insufficient evidence on benefit or risk of routine clindamycin use for treatment of NEC (Faix, Polley, & Grasela, 1988 [B]).

Note: One small randomized controlled trial using clindamycin showed an increase in bowel strictures (Faix, Polley, & Grasela, 1988 [B]).

3. There is insufficient evidence on benefit or risk of oral aminoglycoside use for the treatment of NEC (Hansen et al., 1980 [B]).

## Nutrition

4. There is insufficient evidence on benefit or risk regarding the timing of reinitiating feeding once the diagnosis of NEC has been made.

Note: One retrospective study evaluating the impact of early initiation of feeding (<10 days from diagnosis) suggests a positive impact. Early feeding was associated with a shorter time to full feeds, less catheter related sepsis, and a shorter hospital stay. The study was underpowered to evaluate recurrence risk of NEC (Bohnhorst et al., 2003 [C]).

## Paracentesis

5. Abdominal paracentesis may be helpful to confirm the presence of intestinal gangrene in infants with NEC (Ricketts, 1986 [D]; Kosloske & Goldthorn, 1982 [D]). Indications for paracentesis are absence of pneumoperitoneum and one of the following:
  - Portal venous gas
  - Erythema of abdominal wall
  - Fixed, tender abdominal mass
  - Persistently dilated intestinal segment
  - Clinical deterioration (see Table "Relative indications for surgical consultation" below)

Note: Positive results reliably predict the presence of intestinal gangrene (Accuracy 90% to 97.5%). A "positive" result is considered an aspiration of 0.5 mL of peritoneal fluid and one of the following:

- Yellow-brown or brown staining fluid
- Gram stain positive for bacteria

However, a negative result does not reliably exclude the presence of intestinal gangrene (40% false negative rate) (Kosloske, 1994 [D]; Ricketts, 1986 [D]).

## Surgical Management

### Site of Care

1. It is recommended that neonates with suspected NEC be transferred to a facility that can meet their possible surgical needs if surgical services are not available within the admitting institution. A safe transfer is best achieved when the child is hemodynamically stable. Indications for transfer might include:
  - Pneumoperitoneum
  - Radiographic evidence of portal venous gas (Buras et al., 1986 [D])

(Local Expert Consensus [E]).

2. Note: Evidence suggests that portal gas or diffuse pneumatosis is associated with more severe disease (see Evaluation and Intervention Recommendation #3 below).

### Evaluation and Intervention

2. It is recommended that neonates with clinical/radiographic evidence of pneumoperitoneum be evaluated by a surgeon in a center in which operative intervention can be performed if indicated. Pneumoperitoneum represents an absolute indication for surgical intervention (Tam, Camberos, & Applebaum, 2002 [D]; Kosloske, 1994 [D]; Kosloske, Papile, & Burstein, 1980 [D]).
3. It is recommended that neonates with clinical/radiographic evidence of intrahepatic venous gas (portal venous gas) be evaluated by a surgeon in a center in which operative intervention can be performed if indicated (Molik et al., 2001 [C]; Tam, Camberos, & Applebaum, 2002 [D]; Kosloske, 1994 [D]; Rowe et al., 1994 [D]; Kennedy, Holt, & Ricketts, 1987 [D]; Buras et al., 1986 [D]).
4. The following conditions may be considered as relative indications for surgical consultation in a center in which operative intervention can be performed if indicated:
  - Abdominal wall cellulitis
  - Fixed dilated intestinal segment by x-ray
  - Tender abdominal mass
  - Clinical deterioration refractory to medical management (see Table below)

(Local Expert Consensus [E])

Table 3: Relative Indications for Surgical Consultation

- |   |
|---|
| <ul style="list-style-type: none"> <li>• Persistent metabolic acidosis</li> </ul> |
|---|

- Persistent thrombocytopenia
- Increasing respiratory support
- Increased third-space fluid losses, hypovolemia, oliguria
- Leukopenia, leukocytosis

(Ververidis et al., 2001 [D]; Gupta, Burke, & Herson, 1994 [D]; Buras et al., 1986 [D]; Local Expert Consensus [E])

5. Radiographic signs of NEC have high specificity but low sensitivity, with poor negative predictive values. It is recommended that the decisions regarding surgical intervention be based on both the clinical and radiological presentation. It is recommended that decisions regarding the need for surgical intervention not be made solely on the basis of absent radiographic signs (Tam, Camberos, & Applebaum, 2002 [D]; Kosloske, 1994 [D]).
6. One retrospective study compared the use of the neonatal intensive care unit for surgery versus transport to an operating room setting for neonates weighing less than 1,500 g with severe NEC. Transport of neonates less than 1,500 g from an intensive care unit to an operating room is associated with deterioration in physiologic parameters (Frawley, Bayley, & Chondros, 1999 [D]).
7. The role of percutaneous drainage versus exploratory laparotomy is controversial (Moss et al., 2001 [M]; Ahmed, Ein, & Moore, 1998 [D]; Azarow et al., 1997 [D]; Morgan, Shochat, & Hartman, 1994 [D]; Cheu, Sukarochana, & Lloyd, 1988 [D]). A multicenter, prospective, randomized trial is underway to compare these treatment modalities. No recommendation can be made on surgical approach at the time of publication of this guideline.

#### Definitions:

#### Evidence Based Classifications:

- A: Randomized controlled trial: large sample
- B: Randomized controlled trial: small sample
- C: Prospective trial or large case series
- D: Retrospective analysis
- E: Expert opinion or consensus
- F: Basic laboratory research
- S: Review article
- M: Meta-analysis
- Q: Decision analysis
- L: Legal requirement
- O: Other evidence
- X: No evidence

#### CLINICAL ALGORITHM(S)

None provided

## EVIDENCE SUPPORTING THE RECOMMENDATIONS

### REFERENCES SUPPORTING THE RECOMMENDATIONS

[References open in a new window](#)

### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is classified for the recommendations (see "Major Recommendations").

Evidence Based Classifications:

- A: Randomized controlled trial: large sample
- B: Randomized controlled trial: small sample
- C: Prospective trial or large case series
- D: Retrospective analysis
- E: Expert opinion or consensus
- F: Basic laboratory research
- S: Review article
- M: Meta-analysis
- Q: Decision analysis
- L: Legal requirement
- O: Other evidence
- X: No evidence

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

#### Overall Potential Benefits

- Decreased incidence of necrotizing enterocolitis (NEC)
- Decreased NEC-associated mortality
- Decreased incidence of NEC-associated morbidity

#### Specific Potential Benefits

Infants who received human milk were 4 times less likely to have confirmed NEC compared to infants who received formula. Studies show that providing human milk to twenty preterm infants will prevent one case of NEC.

### POTENTIAL HARMS

- Transport of neonates less than 1500g from an intensive care unit to an operating room is associated with deterioration in physiologic parameters.
- Abdominal paracentesis has a 40% false negative rate for the presence of intestinal gangrene.
- Although radiographic signs of NEC have high specificity, they also have low sensitivity with poor predictive value.

## CONTRAINDICATIONS

### CONTRAINDICATIONS

Conditions that would contraindicate the use of breast milk are detailed in the Pediatric Nutrition Handbook 5th Ed. American Academy of Pediatrics.

## QUALIFYING STATEMENTS

### QUALIFYING STATEMENTS

These recommendations result from review of literature and practices current at the time of their formulations. This protocol does not preclude using care modalities proven efficacious in studies published subsequent to the current revision of this document. This document is not intended to impose standards of care preventing selective variances from the guidelines to meet the specific and unique requirements of individual patients. Adherence to these guideline recommendations is voluntary. The physician in light of the individual circumstances presented by the patient must make the ultimate judgment regarding the priority of any specific procedure.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

The Cincinnati Children's Hospital Medical Center's (CCHMC) Evidence Based Care Guideline on Necrotizing Enterocolitis (NEC) in very low birth weight (VLBW) infants summarizes the evidence to date and outlines a research agenda for increasing knowledge about NEC. Building upon this guideline, a multi-organizational improvement team that included representatives of Cincinnati's three Level 3 Neonatal Intensive Care Units (NICUs) was chartered in spring 2005 to work as a team to decrease NEC incidence through increased human milk (HM) consumption.

The NEC Improvement team is applying a quality improvement (QI) approach to the implementation of recommendations in the guideline. The team is using the Model for Improvement developed by the Institute for Healthcare Improvement, which guides users through developing aims for improvement in NEC rates, HM consumption, and other process measures; testing good ideas on a small scale to see if they lead to improvement; and using simple data collection and analysis strategies to understand the impact of the tests of change. With the support of the National Institute of Child Health and Human Development (NICHD) Neonatal Network, the team will be tracking data related to both NEC incidence and human milk consumption in nearly 100% of VLBW babies admitted to the three NICUs. It is anticipated that HM data will provide a better understanding whether the team's quality improvement (QI) work is leading to improvement in HM consumption, and will also further the knowledge regarding the potential relationship between HM, other factors, and NEC.

### IMPLEMENTATION TOOLS



Foreign Language Translations  
Patient Resources

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT  
CATEGORIES

IOM CARE NEED

Getting Better  
Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2005 Jul 14

GUIDELINE DEVELOPER(S)

Cincinnati Children's Hospital Medical Center - Hospital/Medical Center

SOURCE(S) OF FUNDING

Cincinnati Children's Hospital Medical Center

GUIDELINE COMMITTEE

Necrotizing Enterocolitis Team

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

## Necrotizing Enterocolitis Team Members 2003-2004

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## FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The guideline was developed without external funding. All Team Members and Clinical Effectiveness support staff listed have declared whether they have any conflict of interest.

## GUIDELINE STATUS

This is the current release of the guideline.

## GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [Cincinnati Children's Hospital Medical Center Web site](#).

Print copies: For information regarding the full-text guideline, print copies, or evidence-based practice support services contact the Children's Hospital Medical

Center Health Policy and Clinical Effectiveness Department at  
[HPCEInfo@chmcc.org](mailto:HPCEInfo@chmcc.org).

#### AVAILABILITY OF COMPANION DOCUMENTS

None available

#### PATIENT RESOURCES

The following Health Topics is available:

- Necrotizing enterocolitis/enterocolitis necrotizante. Cincinnati Children's Hospital Medical Center, 2004 Feb. Electronic copies: Available in English and Spanish from the [Cincinnati Children's Hospital Medical Center Web site](#).

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Date Modified: 10/9/2006

